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PHYSIOLOGICAL STANDARDIZATION: ITS VALUE AND LIMITATIONS.

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You have probably heard of the old Irishman who, when asked if he could play the violin replied, "Bedad I don't know; I have never tried." Most men are not so modest in regard to their ability as pharmacologists. It is one of the peculiar traits of the human intellect that there are certain things that almost every man believes he can do as well naturally as those who have made them the pursuit of a lifetime. Among these occupations that are supposed to be Nature's free gift are preaching, boat-sailing and physiological assaying.

It is not mere jealousy, however, that excites the indignation of the professional waterman at the conceit of the amateur sailor, it is the knowledge that human lives are the price of his presumption. So I trust you will pardon me if my language should become emphatic, for you realize as do I that men are paying, if not with their lives, at least with their health, for the ignorance of self-styled pharmacologists.

I shall not attempt, therefore, to discuss with you this afternoon how to make biological assays, for those of you who are trained in the methods of pharmacology need no instruction from me, and to those of you who are not it would be impossible to impart any useful information concerning the biological assay in the short space of a single afternoon. I purpose speaking to you, not as to those who are meditating making these tests themselves but as to those who are

weighing the advisability of introducing such tests into their business and who wish to know the likelihood of the innovation's paying, and are wondering where they can find some one qualified to undertake the work. To such I shall try to give some facts that may serve as an aid in deciding whether the biological assay is of sufficient value to justify the expense involved, by an unprejudiced summary of what in my opinion may and may not be hoped from it.

And first I shall speak of its limitations. We sometimes read of the physiological test being used as a control of the chemical assay. To attempt to corroborate the findings of the chemist by a test on the living animal is about as sensible as it would be for a navigator to regulate his chronometer by an Ingersoll watch; the relative accuracy of the chemical and physiological assay is about the same as that of the $200 chronometer and the dollar watch. The latter is in its place, however, a very useful apparatus; a cheap watch is better than none at all.

The experienced chemist can obtain accurate results because he knows the common sources of error which are likely to vitiate his conclusions and how to guard against them. In biological assay we know only of a few of the possible causes of inaccuracy and even some of these we cannot exclude.

Foremost among the difficulties that destroy the accuracy of the biological test stands that mystery of which we know nothing but to which we give the name of idiosyncrasy. Every physician recognizes well the inexplicable susceptibilities of certain persons to certain drugs, but many scientists forget that man is after all an animal and that the same biological facts hold for the humbler as for the highest type of mammal. After we learn to appreciate this possibility of mistake the only means that we have to guard against it lies in the repetition of experiment sufficiently often that by the laws of chance any exceptional result will not greatly modify the average. Think of a chemist who would make routinely nine or ten assays of the same specimen and then expect an error of 10 or 20 per cent.

Another well-known but frequently neglected fact is that disease has a potent influence on the reaction of the economy to chemical agents. Dogs and frogs are as likely to be sick as are men, indeed more so. It is often quite impossible to recognize an abnormal condition in an animal that you see but once for a few minutes immediately before the experiment; against this fallacy the only defense we have is again the multiplicity of observation.

From external conditions which affect the result it is easier to protect ourselves if we but know those which are likely to influence the effect of the drug under study. The difference in the susceptibility of frogs to many poisons in summer and winter is well known. Edmunds and Hale have conclusively shown the importance of this in the assay of digitalis, and my own experience has convinced me of the futility of hoping for accuracy in the assay of ergot on a hot summer day. There are many other circumstances whose importance may be great but of which we know but little, as age, sex, breed, nourishment, etc. The difficulties arising from imperfect absorption, from the presence of antagonistic principles in crude drugs, of the perversities of inanimate objects, and similar technical obstacles I shall not occupy your time in discussing. I wish to emphasize, however, that even with the utmost care and with frequently repeated experiments we must be prepared for an error of from 10 to 15 per cent. or even more.

Believing as I do that the biological assay is less accurate, more difficult, and often more costly, I cannot see how it can hope to compete with the chemical as a routine means of standardization. But when we recall that there are over a hundred crude vegetable drugs, including some of our most potent poisons, recognized by the Pharmacopœia, for which we have no official process of assay, it is evident that there is need for a subsidiary method of determining the comparative activity of our materia medica. It is probable that for some of these a chemical test will be provided in the next edition of that magnificent work which stands as incontrovertable evidence that in certain lines, at least, the sister professions of America are second to none in the world, but for many of these substances there is little hope that any reliable chemical test will be devised in the near future. Some of them are as unsuited for the pharmacologist as they are for the chemist, but many of them, and especially the more powerful ones, should lend themselves comparatively readily to the physiological assay. Among those which seem pre-eminently suitable for biological standardization I may mention such important remedies as digitalis, squill, apocynum, aspidium, cannabis indica, ergot, gelsemium, lobelia, and veratrum, etc. If I can show you that the pharmacologist is able to solve many of the vexatious pharmaceutical problems that cling to these drugs, will you not grant me that he is worthy your most earnest encouragement in his work?

Let us try, therefore, to peer into the future and see what prospects of success lie before him who embarks on this enterprise. We can hope to penetrate the dark mist which hides from our vision what is to come, only through the telescope of history, and as a foundation for the prophecy of the destiny of biological assay I wish briefly to review with you some of the past accomplishments of the art.

Before we seek to gauge the progress that has been made we must have a clear understanding of the goal towards which we are striving, of the questions which we may hope to answer by the method. First and foremost of course we desire a means of determining the relative potency of individual samples of drugs; in other words, to be able to distinguish between a specimen of good quality and one of poor grade. But allow me to emphasize with all the vigor that I can that this is not the ultimate nor even the chief aim of the real pharmacologist. The idea which is prevalent, that when a pharmacologist has worked out a method of assay simple enough to be commercially available and accurate enough to be scientifically useful, he has fulfilled his whole duty to the pharmacist, is an error due I believe largely to the commercial dominance in the field of investigation.

The man who is engaged in the drug business as a business is satisfied if his pharmacologist enables him to sell reliable goods, that is, to manufacture preparations of uniform strength; but the scientific pharmacist wishes an answer to many and various questions that have been perplexing his profession for years. He wants the biological assayer to aid him in discovering the most favorable condition under which the plant may be grown and the best method of collecting and preserving the crude drug; the most useful solvent for extracting its activities; the rate of deterioration which takes place both in the crude drug and its galenicals, and the methods of delaying these changes. Last but by no means least the pharmacologist can be of invaluable assistance in working out methods of chemical standardization.

Keeping these objectives before us, let us briefly review what has been accomplished with some individual drugs along the lines I have mentioned.

Because of its great practical importance, and of its well-known liability to variations, and because it produces certain well-marked effects which would seem to make it an especially suitable object for physiological testing, digitalis has been more studied from the

standpoint of biological standardization than any other drug. As long ago as 1866 Fagge and Stevenson attempted to determine the relative activity of several members of the digitalis group by their toxicity to frogs. Their studies, however, were undertaken chiefly with the idea of comparing bodies closely allied physiologically to digitalis, as antiarin, helleborein, and the like, rather than preparations of digitalis itself. Apparently it was fifteen years later that the idea of using a similar method for determining the quality of preparations of digitalis was first projected. In the year 1881, two papers were published upon this subject, one by Bennefield, who used a method based upon the quantity of digitalis required to kill a rabbit, and the other by Frankel who based his calculations upon the changes caused in the movements of the dog's heart. It is not my purpose to enter into the vigorous discussion which has been waged as to the relative value of different methods of standardizing digitalis; I wish only to express my conviction that no method of biological assay, the conclusions of which are expressed in units of a standard preparation, can be held to be satisfactory. The result of the physiological test must be such that it can be expressed in absolute language, perhaps like that which is used to express the standard for diphtheria toxin: the amount required to kill a certain weight of a certain animal in a given period of time, and under conditions which are accurately described.

The first result of the physiological assays of digitalis was to yield scientific proof of a fact that was already shrewdly guessed, namely, that different samples of the drug varied enormously in their potency. It has been shown by a large number of investigators that the ordinary range of variation of different specimens of digitalis is anywhere within a limit of 400 per cent. That is, that the strongest sample will be about four times as active as the weakest. Farr and Haynes found that the prejudice in favor of the second year leaves of the Digitalis purpurea is only partially justified; for while it is true that in the samples they examined the leaves of the second year's growth were slightly more active than those of the first year's growth, the difference was only as 8 to 10. Focke has shown that the leaves of the wild digitalis are more potent than those of the cultivated plant, and in the samples he examined Ott found that those which came from Bohemia were more potent than those from other parts of Europe. Wolff found that the deterioration of the crude digitalis leaves was due almost solely to improper methods

of storing; if the leaves were dried in vacuo at a temperature of about 100° and afterwards hermetically sealed, they retained their activity unimpaired for a long period of time. Dixon and Haynes were unable to observe any deterioration in a tincture of digitalis which was kept for four months without special precaution. Houghton found, however, that the present official liquid preparations of digitalis lost about 10 per cent. a year, although the tincture of strophanthus seemed permanent. A higher percentage of alcohol than at present required seemed also to be shown by his work to be desirable.

Bennefield made an attempt to determine the quality of digitalis tincture by the percentage of the solid extractive matter which it contained, but found that this bore no relation to the physiological activities of the drug. In 1895 Keller described a method for the chemical assay of digitalis, based upon its percentage of digitoxin. Ziegenbein, and also Famulener and Lyons, found, however, by means of biological tests that Keller's method of assay was unreliable. In 1904, Barger and Shaw confirmed these findings, and showed that the inaccuracy of Keller's method depended upon three facts: first, that it did not extract all the digitoxin; second, that it did not isolate the digitoxin in a pure condition; third, that digitoxin is not the only active ingredient of digitalis. Which reminds me of the story of the little girl, who when asked if she was going to Maggie Jones's party said, "No, she did not like Maggie Jones, she had nothing to wear and besides she was not invited."

This hasty summary of what has been done through biological assay of digitalis seems to me to show great advancement in our knowledge of an extraordinary complex subject, for while we may be disappointed at the slowness of the progress it is undeniable that great advance has been made. Of the questions which we saw were within the province of the assayer to consider, all have been answered, if not with absolute finality, yet within the limits of scientific probability, except only the means of standardizing the drug chemically. He has told you how you may distinguish between active and feeble samples of digitalis, he has told you where grow the best quality of leaves, when to gather them and how to keep them with the minimum of deterioration, he has told you the best menstruum to extract their virtues and of the necessity of dating digitalis galenicals. I am convinced that did the pharmacist but hearken to the advice of the pharmacologist as to the manufacture

of these preparations the clinician would cease to complain as to the quality of the tincture of digitalis which is dispensed to his patients.

Another drug which has attracted attention as a worthy object of physiological assay is ergot. The earliest effort to ascertain the quality of ergot by biological means appears to have been made by Grünfeld with the method suggested by Prof. Kobert, of determining the dose necessary to interrupt the circulation in the comb and wattle of the rooster. Little practical use was made, however, of the biological method in connection with ergot until 1898, when Houghton published an account of some results of cock's comb assays practiced commercially. The workers with this drug have not been nearly so numerous as in the case of digitalis and the results are correspondingly meagre. Beyond the mere proof of the variability of galenical preparations of ergot almost nothing of value was added to our knowledge of this drug until within the last few years; from a pharmaceutical standpoint no more was known of ergot at the opening of the present century than fifty years ago.

Within the last three or four years, however, it has been the subject of more study and some very interesting facts have been brought to light by the work of Kraft, of Barger and Dale, of Edmunds, and others. In the experiments which have been going on in the pharmacological laboratory of the University of Pennsylvania during the past two years we have been able to show that the inferior quality of the fluidextract of ergot which is at present on the market is due largely to changes which take place after its manufacture; even in hermetically sealed bottles the loss of potency is at the rate of about 3 per cent. a month, and if the preparation is not guarded from contact with the air the deterioration may amount to 50 per cent. in a few weeks. Our recent evidence, although not conclusive, inclines us to the belief that, contrary to the popular opinion, the crude drug does not weaken so rapidly as the fluidextract. We have also worked out a method of chemically determining the quality of ergot which has so far yielded us figures fairly parallel to the results of physiological tests of the drug.

I should like to mention one other individual example, very briefly, of progress in a pharmaceutical subject through physiological methods; not so much because of the importance of the drug in question as for an evidence of what can be accomplished by a single

capable worker in a comparatively short space of time. I refer to the contributions which have been made by Dr. Reid Hunt to our knowledge of the thyroid gland. In two interesting communications, published within a year of each other, Dr. Hunt described a method for standardization of the thyroid gland based upon principles which were absolutely new to biological assay; showed the wide extent of variations in the commercial samples of the drug; showed that the activity of the thyroid body varied not only with the species but with the age of the animal from which the glands were obtained, and the influences which special feeding of the animal may have upon the activity of the gland; and, finally, determined that with unsophisticated glands the percentage of iodine was an accurate indicator of the quality of the drug. Truly, through this one man's efforts we have been led with dramatic suddenness from absolute darkness to the brilliancy of almost complete knowledge.

I have chosen as examples of what may be accomplished three drugs which have yielded some interesting results, but I must confess that outside of these instances which I have mentioned little of importance has been added to our knowledge of practical pharmacy through physiological investigation. When we consider how much might have been done, and how little has been done, the pharmacologist may well bow his head in shame at the neglect of so fruitful a field. We cannot plead that the idea of biological assay is so recent that there has not been time enough for its development. More than forty years have elapsed since the method was earnestly suggested and for more than twenty-five years it has been more or less systematically applied in various laboratories of the world. There certainly has been time enough in this half century of an intellectual progress, whose rapidity has never been equalled at any stage of the world's history, for the development and application of the method of biological assay to a dozen drugs instead of one or two.

But the laborers in this field have been so pitifully few that one should wonder not at the smallness of the harvest but at its abundance. We are, however, not altogether without excuse for the neglect of this field. Pharmacology is a young science—men sometimes forget that the first pharmacologist in the modern sense of the word is still living and teaching—and in the enormous mass of problems the accumulations of centuries, many of them of fundamental importance for its own development, which the world hurled

at the infant science, it is little marvel that some have been neglected. And even to-day the little handful of men who are working in this line are being assailed on every hand to answer the widest variety of questions. We are supposed to tell immediately the exact physiological effects of new synthetics which are being dumped upon the profession by the wagon-load, to discover the laws which govern the relation of chemical composition to physiological action so that the chemists may dump their synthetized garbage upon us still more rapidly, we are asked to discover at once specifics for various fatal fevers which the growing intimacy with the tropics has made so important to civilized peoples, to furnish the means to the physiologist and pathologist for solving some of the obscure problems of their branches, to explain to the clinician the mode of action of the ancient remedies, and to convince him of the worthlessness of drugs whose inertness is hidden beneath the traditions of antiquity or the glitter of the advertiser's gold, to suggest new uses for old drugs and new drugs for old diseases, to—— Can you contemn pharmacologists that they have failed to recognize the importance of biological assay to practical medicine?

As a result of this the development of the physiological assay has been left largely in the hands of the manufacturers and they have been more interested in developing it as an advertising asset than as a means of standardization. This may seem a rather sweeping accusation but I think it no great exaggeration. You would think it strange, to say the least, if a manufacturing pharmacist were to entrust all his chemical work to a young man with no more experience than is gathered in the ordinary course in a pharmaceutical college; and if this same manufacturer were then boastingly to advertise his chemical control of all his products you would hardly hesitate to criticize. Yet the situation in many of the so-called pharmacologic departments of wholesale druggists is even worse than this. You know that practical experience is necessary before a man can be trusted to turn out reliable chemical assays, no amount of book learning can take the place of the actual manipulation of the process. If this is true of chemical work in which we can put down in black and white the difficulties one is likely to encounter, how infinitely more necessary is practical experience in a field where we know almost nothing of the way in which we may go astray, where reliable methods have not even been worked out, and where we are

dealing with a living reagent of whose delicacy of response we can never be sure.

"But," say these men in defense, "it is not because we do not want them, but because we cannot get them, that we do not have competent experts in this line." To this I reply that the reason the manufacturers cannot get trained pharmacologists is because they will not pay the necessary price. I confess that at present the cost is large. The demand for pharmacologists to-day is greater than the supply and as is always the case in such conditions the price is high. Suppose a young pharmacologist holds a position at a university and is earning say $1500 a year, with congenial surroundings and good prospects for advancement, would he not be a fool to change such a position for a commercial one with the attached obloquy which justly or unjustly is associated with such work, in which the likelihood of further advance is remote, for practically the same financial recompense he is receiving for his university work?

To tempt the scientist into commercial work requires two things: a larger salary than he is likely to receive for educational labor and a readjustment of the conditions which maintain in the laboratory of the drug manufacturers. He must cease to be regarded as a sort of attache to the advertising staff and be allowed at least a degree of scientific freedom. One of the chief reasons for the odium which pharmacologists consider inseparable from a commercial position is that the investigator must publish nothing or only that which his employer considers to be to the advantage of his business interests; in other words, his work is limited not only as to its kind but also as to the results he shall obtain. Need I tell you that such a situation is utterly abhorrent to any man of scientific instincts?

I see no reason why this last trouble should not be easily eradicated; just inject a little really ethical integrity into your business and the matter is arranged. As to the monetary question, I am not in a position to tell you whether you can stand the expense and continue to do business or not, that you must answer for yourself.

If not, the problem becomes difficult, but it must be solved. If the next edition of the United States Pharmacopœia includes more biological tests, and there is evidence of a growing sentiment in this direction, either the manufacturer will have to find some one to make these tests or else stop making preparations of these drugs; for if I read the times aright the inexperience of their experts is not going to be accepted by the Government as an excuse for the failure

of their products to come up to the standard. Either the assay must be done rightly or the manufacturer is going to have trouble with the law.

While the number of drugs which require biological assay may seem at first thought too small to justify the outlay necessary to obtain a man competent to do the work, there are so many other ways in which a pharmacologist may make himself valuable, as, for instance, the introduction of new drugs and new preparations, that there is at least a strong possibility of such an expert being a paying investment even at present prices. If the manufacturer can afford to pay these necessary salaries let him step right up and do so and the dilemma is evaporated.

If he cannot, I see but two possible alternatives: either the manufacture of preparations of digitalis and other drugs which shall be biologically assayed will have to be left in the hands of the specialists, as antitoxin is now, or else some artificial means of increasing the supply of pharmacologists will have to be adopted.

To fulfil this latter the first step is to provide some place where the willing novitiate can obtain his education. At present the training of a pharmacologist is almost universally an individual one; that is, some young seeker for knowledge enters into the laboratory of some older man who has previously trod the same path and labors and patiently accepts the simpler duties which he is fit to perform, watching his senior and gradually imbibing little by little a working knowledge of the art; much the same process of education as the old fashioned apprentice was led through in the bygone days. Whether or not our modern more systematized and more rapid method turns out any better or as good workmen is a question open to debate, but at least it turns them out more rapidly, and quickness is the great desideratum in the eyes of the young America of to-day. The change of conditions occasioned by the passage of the various food and drug acts all over the country, and the consequent compulsion to abide by the standards in fact as well as in name, has led to the formation of courses intended for the training of experts in this line similar to the one established a year or two ago at this venerable College for nearly a century the pioneer in all movements looking to the uplift of the profession of pharmacy.

But who is to give a course of training in methods of biological assay? Are the schools of medicine likely to do so? I think not, for while I grant you they are at present the best equipped institu-

tions for such work, the medical profession generally does not feel the pinch of necessity with quite the same sharpness that do the pharmacists. Will the schools of pharmacy undertake the task? Can they? I hardly think so unless some special aid is rendered them. Pharmacists generally speaking, teachers, retailers, and wholesalers, are only beginning to appreciate that under modern conditions *all* education has become a matter of philanthropy, not to say charity. The world has long believed that a young man should be offered as much as he wants of general education and culture, at his own price, as is shown by our public school system, with its normal schools and high schools, and by our numerous partially endowed colleges. But we of to-day have gone a step further than our fathers and are giving young men not only their general education but are giving them their technical training fitting them for their life-work, free of cost. You find the great universities of the land supporting their chemical departments, their engineering courses, their medical schools, etc., each being run at a large annual loss, and their continued existence made possible only through the aid of their alumni and friends. But the schools of pharmacy are attempting to struggle against this universal trend, to keep up the standard of their profession and yet make those who enter it pay for the privilege. It is a lost cause; either you must be content to see the apothecary little by little degenerate into a minor merchant, or you must come to the financial assistance of your institutions of learning. There is no more practical way to begin than for you who most poignantly feel the need of pharmacologists and who have been able to gather the means for the satisfying of your ambitions to establish in connection with your alma mater a post-graduate department for the training of young men for this work. The necessity is yours, the opportunity is yours, what will you do with it?

ASSAY OF MEDICINAL PLASTERS.

By Frederick B. Kilmer.

Comparatively little literature has appeared in scientific publications in respect to the analysis or assay of medicinal plasters made with an India rubber base.

The enactment of the Federal Food and Drugs Law and the

enactment of similar laws in the various States has brought the subject to the attention of the pharmaceutical chemist, and at the present time the subject is one of moment to both the medical and pharmaceutical professions.

Prior to the issuance of the last revision of the Pharmacopœia, no authoritative process of assay of any medicinal plaster appeared in that work. In this revision a process was given for the assay for mydriatic alkaloids in belladonna plasters made with a rubber base. Those who have given attention to the subject will no doubt agree with the statement that has been made, that it is a very difficult matter to assay some kinds of medicinal plasters made with a rubber base. It is a well-known fact that for some such plasters no method is known for the assay of the drugs contained therein, for the reason that the drug used has no alkaloid, or no alkaloid or no inorganic substance capable of definite measurement.

In other varieties of these plasters the presence in the rubber base of resinous or other matters is such as to confuse the results and make them of doubtful value. In the laboratory of the writer considerable work has been done in the assay of this class of preparations, and in our work we possess some advantages over any outside laboratory, in that as the laboratory is connected with the manufacturing department it is at once known exactly what has been put into a plaster, and it is only necessary to provide methods of assay that will give the results looked for. The methods and processes which I herewith present are simply those which have been worked out in the laboratory, more particularly as a check to manufacturing processes. They are presented for what they may be worth, with the hope that other workers may have an opportunity to try them and thus bring out information of value to those interested.

BELLADONNA PLASTERS.

For belladonna plasters we use the assay method of the eighth revision of the United States Pharmacopœia. This process, with some slight modifications, has been entirely satisfactory in our laboratory, where assays running perhaps into thousands have been performed. It has also had the benefit of an extended check test, in that in this laboratory it is our practice to first assay the drug used in the manufacture of the plaster and then the solid extract made from the drug; the mass itself is made up of the assayed extract taken in an amount which will give in the finished product the desired percentage

of alkaloid required in the plaster, and by this method of plaster assay the results have shown that in mixing several hundred pounds the assayed plaster corresponds with the calculated amount, often to the second and third decimal.

SALICYLIC ACID PLASTER.

The method which we use for the analysis of salicylic acid plaster is a colorimetric method with ferric chloride. The depth of color imparted to a ferric chloride solution by a measured amount of a solution of the plaster is compared with that of a measured quantity of a standard solution of salicylic acid of known strength. Colorimetric methods are always subject to some variation, chiefly on account of errors of eyesight; but because of the presence of resinous materials in rubber plaster masses, no other method has been found to be satisfactory and we have found that in our hands, by careful manipulation, this color comparison method has given sufficiently satisfactory results.

Plaster Solution.—Weigh out accurately about 5 Gm. of the plaster cut into rather small strips. Place on the table two beakers of about 150 c.c. capacity each. Designate them as No. 1 and No. 2. Place the weighed strips of plaster in No. 1. Add to it 50 c.c. of chloroform. Stir gently until all the compound is removed from the plaster-cloth and in solution. Pour the syrupy solution into beaker No. 2. Add to this in No. 2 beaker, 40 c.c. ordinary 94 per cent. alcohol, stir thoroughly to precipitate and coagulate the rubber and allow it to stand. Pour off all possible of the liquid into a glass stoppered graduate 250 c.c. flask. The rubber should be worked up into a compact mass so that no particles are carried over when the liquid is poured off and all possible liquid should be pressed out of the mass with a glass rod. To the plaster-cloth in beaker No. 1 add 25 c.c. chloroform. Stir carefully and thoroughly until all the remaining plaster-mass is dissolved from the cloth and sides of the beaker. Again pour off the solution into beaker No. 2, which contains the precipitated rubber. Work up with glass rod until all of the rubber mass is again in solution in the chloroform. Now re-precipitate the rubber from this solution with 20 c.c. alcohol, working up with rod and pouring off as before, mixing the fluid with the first portion in the flask. Once again wash the cloth in beaker No. 1 with 25 c.c. chloroform. Pour off into No. 2 beaker, dissolving again the rubber mass in it. Re-precipitate the rubber from

it with 20 c.c. alcohol as before, pour off and mix the decanted fluid with the other two portions in the flask which now contains all of the salicylic acid in solution. Fill the flask up to the 250 c.c. mark with alcohol. Remove the cloth, which should now be white and clean, from beaker No. 1, allow it to dry spontaneously, and weigh. Subtract its weight from the total weight of plaster used, thus ascertaining the weight of plaster compound taken for assay.

Standard Salicylic Acid Solution.—Weigh out exactly 0.5 Gm. pure salicylic acid and dissolve it in 50 per cent. alcohol. Transfer to a 500 c.c. glass stoppered graduated flask, rinse out the vessel, in which the acid was dissolved, with repeated portions of 50 per cent. alcohol, adding each portion to the solution in the flask. Make up to the 500 c.c. mark with 50 per cent. alcohol, shake thoroughly. One c.c. of this solution contains .001 Gm. salicylic acid.

Analysis by Color Comparison.—For this work we use two large test-tubes of similar internal diameter (1¼ inches by 6 inches long). Any pair of glass cylinders or tubes will suffice, but small diameter test-tubes do not give sufficient thickness of solution to secure enough depth of color with transmitted light. Place these tubes side by side. In a beaker place 100 c.c. distilled water to which add one drop ferric chloride solution U.S.P. Stir the liquid and pour into each of the test-tubes 50 c.c. of it. Designate them No. 1 and No. 2. Now add to No. 1 tube from burette, sufficient of the standard salicylic acid solution to give a strong clean wine color. Stir with a glass rod after each addition of the acid solution. Multiply number of c.c. used by .001, which will give the weight in grammes of salicylic acid used in tube No. 1—the standard. Now add to tube No. 2 from another burette sufficient of the plaster solution exactly to match the color obtained in tube No. 1. This plaster solution must be added a little at a time and the solution in the test-tube well stirred with a glass rod after each addition. When the matching point is nearly reached it may be necessary to filter off the contents of the test-tube No. 2. Clean the tube and replace the fluid, proceeding thereafter to add the plaster solution a drop at a time. The reason for doing this is that the small amount of resinous matter separated from the solution may cloud the mixture in No. 2 test-tube and interfere with the color judgment. By closing one eye and observing the colors while holding the tubes side by side between the eye and a window the colors can be matched very closely. It is obvious that the quantity of plaster solution used

contains the same amount of salicylic acid as was used in tube No. 1. That quantity is already determined by means of the standard solution. Therefore 250 (total amount of plaster solution) divided by the number of c.c. plaster solution used in tube No. 2 and the result multiplied by grammes acid found to have been used in tube No. 1 gives the weight of acid in the plaster compound. Multiply the weight of the salicylic acid found by 100 and divide the result by the weight of the plaster compound used. The result is the per cent. of salicylic acid present.

This method has been used chiefly with plasters containing 20, 25, and 30 per cent. of salicylic acid. When very small percentages are present it will, of course, necessitate the addition of a much larger quantity of plaster solution to tube No. 2 in order to secure the same color as that of No. 1 tube and consequently the color of tube No. 2 will be unduly diluted. If by trial this is found to be the case, it will be necessary to prepare a weaker standard solution or else a more concentrated plaster solution. This matter can readily be determined by trial.

In making these assays it is well to make three of each and to take the average. By doing this we have been able to get satisfactory results, the natural variations of color judgment balancing one another and the result being nearly correct in the average of the three determinations from one lot of plaster solution.

MERCURIAL PLASTER.

The requirement of the U.S.P. is that this plaster shall contain 30 per cent. metallic mercury.

Method of Assay.—Weigh out about 5 Gm. of the plaster, cut it into rather small strips. Place these in a beaker and add about 50 c.c. benzol. Stir well for some time to soften and dissolve the compound. Pour the solution off into a beaker of about 200 c.c. capacity, allowing the cloth to remain in the first beaker. To the cloth in the first beaker add repeated portions of about 50 c.c. benzol, stirring well and pouring off each time into the second beaker until the mixed solutions amount to about 200 c.c. The clean cloth is now allowed to dry in the air, weighed, and its weight subtracted from the weight of the plaster taken. This gives the weight of the compound used.

The mixed solutions of the compound, measuring about 200 c.c., are now well stirred and then allowed to stand covered in a tall

beaker until all the gray metallic mercury has settled to the bottom. This usually is accomplished in about twenty-four hours. Chloroform can be substituted for benzol in this dissolving operation, but benzol is used in our work on account of its relative lightness, because of which the mercury settles more quickly.

When the gray mercury has settled out pour off carefully the supernatant benzol which contains the rubber and resins in solution. On account of the high gravity of the mercury the benzol can be decanted until nothing remains but a slime of mercury powder. To this add at once one or two c.c. of aqua regia, warm it, stir, and let stand. If all gray color is not removed in about an hour add another c.c. of aqua regia, stir, warm, and let stand again, repeating the operation, if necessary, to dissolve all of the mercury. Use, however, as little acid as possible so as to avoid all but a slight excess, for much excess will interfere with the subsequent precipitation of the mercury by means of H_2S. When the acid solution has lost all gray color, indicating the complete solution of the mercury, add about 50 c.c. water. Stir, and filter through a paper filter containing a tuft of absorbent cotton. The cotton catches the flocculent particles of resinous matter and prevents stoppage of the filtration by clogging. Rinse out the beaker with repeated portions of water, which is poured through the filter. Continue until about 200 c.c. of filtrate is secured. Place this filtrate in an Erlenmeyer flask of ample capacity, pass H_2S through it until the mercury is all precipitated as black HgS. Let it settle a few minutes and filter at once through a weighed filter paper of fine texture, wash the precipitate on the filter with a little water and dry at 100° C., cool, and weigh. Subtract the weight of the filter paper and calculate the resultant weight of the mercury sulphide to mercury, viz.:

$$232 : 200 = \text{wt. HgS} : x \text{ wt. mercury.}$$

The weight of mercury found multiplied by 100 and divided by the weight of the compound used gives the per cent. of mercury in the compound.

AMMONIAC AND MERCURY PLASTER.

The requirement of the U.S.P. is that this plaster shall contain 18 per cent. metallic mercury.

Method of Assay for Mercury.—This is the same as with mercurial plaster.

STRENGTHENING PLASTER.

Assay for Iron.—Weigh out accurately two pieces of plaster of about 5 Gm. each, cutting them side by side from the same piece in order that the relative amount of compound to cloth will be the same in each piece.

Dissolve off the compound from one of the pieces with repeated portions of chloroform until the cloth is clean. Allow the cloth to dry spontaneously and weigh it. Multiply its weight by 100 and divide by the total weight of plaster used. This gives the per cent. of cloth in the plaster, the figure so obtained to be used later.

The second piece of plaster of known exact weight is placed in small clippings in a porcelain crucible and ignited. Dissolve the residue in warm concentrated hydrochloric acid, dilute to about 200 c.c. with water, and filter. Pour the solution into a porcelain dish, heat nearly to boiling, and add ammonia in excess to precipitate the iron as Fe_2OH_6. Allow the precipitate to settle, decant on to a paper filter of known low ash value, wash the precipitate with hot water, and dry. This is now ignited in a weighed porcelain crucible with lid, the iron hydroxide being first carefully scraped from the filter and ignited alone in the crucible and the paper containing only a little adherent hydroxide is ignited separately on the lid of the crucible. When the paper is completely reduced to ashes, the lid is placed on the crucible and both are transferred to a desiccator to cool. When cooled, weigh and subtract the weight of the crucible and lid from the weight of the same with contents. This gives the weight of iron oxide (Fe_2O_3) contained in the crucible.

This is calculated to metallic iron, viz.:

$$160 : 112 = \text{wt. } Fe_2O_3 : x \text{ wt. Fe.}$$

The percentage of cloth in the plaster has been determined as above in other piece of plaster, therefore the weight of the piece of plaster ignited is multiplied by the per cent. figure for cloth, determined in the other piece of plaster. The weight so found is subtracted from the weight of plaster ignited, which result is the weight of compound ignited.

The weight of Fe found, multiplied by 100, and divided by the weight of compound ignited gives the per cent. of Fe in the compound.

To Arthur W. Clark and Powell Hampton acknowledgment is due for work in the elaboration of these processes.

THE CHEMICAL ASSAY OF FLUIDEXTRACT OF ERGOT.

By John R. Rippetoe.

Dr. Horatio C. Wood, Jr., has recently shown (Am. Jour. Pharm., **81**, p. 215, May, 1909) that the benzol extract of the fluidextract of ergot bears a proportional relation to its physiological action. Dr. Wood's physiological tests were made by the blood-pressure method.

The writer for the past three years has been testing the fluidextract by observing the action upon the cock's comb. Although the method is considered by most workers to be of little value, a marked difference is noted between fresh and old preparations. A fluidextract made from a drug of good quality, when injected into the thigh muscle of a Plymouth Rock rooster in a dose of 1.5 c.c. to one kilogramme bodyweight of rooster produces characteristic physiological reactions; the breathing is dyspnœic, the wings are drooped, there is stupor, diarrhœa, and the wattles and comb become pale and then bluish-black in color. The dyspnœa usually passes off within three to five hours and the comb becomes normal within six to eight hours. After one year or more the preparation requires a larger dose to produce the same results. Apparently, so far as the action on the rooster is concerned, the preparation has deteriorated.

Some of the preparations tested as above in the past have been recently assayed by Dr. Wood's benzol-extract method, the method having been modified as follows: Introduce 10 c.c. of the fluidextract into an eight-ounce bottle, add 20 c.c. water and 100 c.c. benzol. Shake the mixed liquids in a mechanical shaker for thirty minutes. Allow the liquid to stand until the benzol solution is clear. Decant 50 c.c. of the benzol solution, evaporate, and dry the residue to constant weight on a water-bath at a low temperature.

	Date When Fluidextract Made.	Test on Rooster. Date.	Result.	Benzol Extract. Oct. 1909.
A	June, 1907	July, 1907	Good	0.14 Gm. in 100 c.c.
		Feb., 1908	Poor	
B	Nov., 1907	Feb., 1908	Good	0.20 Gm. in 100 c.c.
		Dec., 1908	Poor	

C. May, 1908	June, 1908	Good	0.26 Gm. in 100 c.c.
	Jan., 1909	Poor	
D June, 1909	July, 1909	Good	0.55 Gm. in 100 c.c.
Alcoholic-drug extract	Dec., 1908	Good	0.56 per cent.
Glycerin-drug extract	Dec., 1908	Very poor	0.09 per cent.

The preparations were considered of "poor" quality when they required a 25 to 50 per cent. increase in the dose to produce the characteristic reaction of a preparation passed as "good." Each preparation was tested in duplicate, using two roosters and using the roosters for only one test. The samples marked alcoholic and glycerin-drug extract, were prepared and used for comparison of alcoholic and glycerin menstruums as reported by me in a paper published in the AMER. JOUR. PHARM., **81**, p. 85, Feb., 1909.

While no previous assays of benzol extract were made on the samples, it is of interest to note that they contain a proportional lower amount of extract according to their age. It is also noted that the preparations after eight months' aging required larger doses to produce the desired action upon the cock's comb.

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THE NEW ITALIAN PHARMACOPŒIA.

BY M. I. WILBERT, Washington, D.C.

Farmacopea Ufficiale del regno d'Italia, terza edizione, is the official title of the new Italian Pharmacopœia bearing the imprint: "Roma Tipografia delle Mantellate, 1909," and advertised to sell for Lire 5 (about one dollar).

Coming as this book does shortly before the convening of our own Pharmacopœial Revision Convention, a review of some of the more characteristic features may perhaps be of interest as suggestions for innovations to avoid or to adopt.

The book is printed in Italian with Latin sub-titles and contains a total of xiv and 452 pages, 8vo. As a pharmacopœia it contains an innovation in the shape of an "Elenco" containing descriptions of proprietary preparations, including a total of 91

titles; several of these titles, however, include a long line of preparations, such as hypodermic solutions and medicinal granules.

The official descriptions from the "Spirit of Minderer" (Acetato di Ammonio) to "Sugar" (Zucchero) cover a total of 340 pages and aggregate 659 titles or monographs: 17 animal drugs, 158 vegetable drugs, 195 chemical substances, 257 pharmaceutical preparations, and 18 general descriptions or formulas.

For the student who is not well versed in Italian this book is rather difficult to consult, as it is arranged alphabetically according to the Italian titles.

Thirty titles were deleted and 54 new titles added. Among the new additions we find such old and new friends as acetyl salicylic acid; adrenalin, diethymalonylurea, hexamethylene-tetramine, ether for anæsthesia, silver fluoride, quinine ethylcarbonate, sodium formate, sodium glycerophosphate, calcium glycerophosphate, pyramidon, methyl salicylate, stovaine, talcum, trional, quinine tannate, trioxymethylene, seidlitz powder, and wine of antimony.

The provisions of the International Congress for the unification of the formulæ of potent medicaments are closely adhered to and all of the titles included in the Brussels protocol are designated (F. I.) "formola internazionale." The international drop counter is recognized and a table added giving the number of drops of official preparations necessary to weigh one gramme, also the weight of one drop in milligrammes.

Many of the monographs include two or more drugs, thus under "arnica" we find descriptions of "arnicæ flores et rhizoma" and under "arancia amaro" descriptions of "aurantii amari cortex, flores et folia." The botanical descriptions are general rather than detailed and there are comparatively few tests included in the descriptions for vegetable drugs.

The titles of official preparations are all enumerated under the descriptions of the drugs and chemical substances.

Volatile oils are classified under the general heading "Essenze," "olea volatilia" and the related aromatic waters are directed to be made, by distillation, from the drug itself.

Among the more novel pharmaceutical preparations are granules of aconitine, of arsenous anhydride, of strychnine nitrate, and of atropine sulphate, also ophthalmic discs of atropine, of cocaine, and of eserine.

Under elixirs we find but a single title "elixir acidum hallerii,"

a mixture of equal parts, by weight, of concentrated sulphuric acid and 90° alcohol.

Fluidextracts are represented by four formulas—"segata cornuta" (ergot), "hamamelis," "idraste" (hydrastis), and "cascara sagrada."

Decoctions and infusions are still liberally represented. Under the general heading "Decotti-Decocta," we find ten additional formulas and under the general heading "Infusi-Infusa" we find no less than eighteen additional formulas, two of these latter preparations are compound preparations, one practically the equivalent of the aqueous tincture of rhubarb of the N. F. while the other is an infusion of senna with manna.

Under "Sterilizzazione" we find a comprehensive monograph on sterilization, including directions for sterilizing with and without an autoclave and notes directing attention to some of the precautions that are necessary to prevent decomposition of such substances as cocaine, morphine, and eserine.

Maximum single and daily doses are appended to the more potent articles and the preparations containing them and these doses are again presented in the form of a table in the Appendix to the pharmacopœia.

Among the remaining, more or less interesting, tables that are appended we find a list of reagents and volumetric solutions and a list of indispensable chemical apparatus, a list of medicaments that must be in stock, and also a list of the pharmaceutical apparatus that must be in each pharmacy, and finally the protocol of the Brussels Conference for the unification of the formulæ of potent medicaments.

The index is rather a comprehensive one and includes thirty double column, closely printed pages.

In conclusion it may be said that the Italian Pharmacopœia, in common with practically each one of the recently published pharmacopœias of the Latin European countries, is a curious jumble of the old and the new. It represents a survival of antiquated and obsolete drugs and preparations with modern ideals for international standards and an unusually great number of the newer remedies.

It recognizes the value of sterilization and is the only national pharmacopœia to recognize and describe proprietary mixtures. Taken altogether, however, the book is a creditable one indeed and reflects erudition and ability both on the part of the medical practitioners and the pharmacists for whose use it is designed.

PROGRESS IN PHARMACY.

By M. I. Wilbert, Washington, D. C.

A QUARTERLY REVIEW OF SOME OF THE MORE INTERESTING LITERATURE RELATING TO PHARMACY AND MATERIA MEDICA.

Not for many years have the happenings in the pharmaceutical line attracted such wide-spread attention and discussion as at present, and, if interest is an indication of importance, pharmacists who can manage to keep abreast of the progress that is being made are destined to come into their own in the near future.

The interest in the forthcoming Pharmacopœial Convention is growing. Both medical and pharmaceutical journals are devoting considerable space to the consideration of matter relating to the Pharmacopœia. As the time for the convention approaches, we also find an ever-increasing difference of opinion on the scope and content of the Pharmacopœia manifesting itself. One extreme, in this connection, is that embodied in the so-called Coudrey Bill.

The U.S.P. and the Coudrey Bill.—Some of the daily papers and many of the medical and pharmaceutical journals have recently devoted considerable space to the discussion of a bill introduced in the House of Representatives on December 10, 1909, by Representative Coudrey. This bill is officially designated as H.R. 13859, and it provides for the amendment of the Pure Food and Drugs Act of 1906 so as to require "That the United States Government should edit and publish the United States Pharmacopœia or the National Formulary, and have a complete test for purity and strength of all drugs and chemicals whether generally used or not."

Dr. H. H. Rusby (*A. Ph. A. Bulletin*, 1910, p. 82) recently expressed the belief that the Pharmacopœia being a national standard should include all drugs that are used to any considerable extent. He also believes that a new class of drug standards will be essential. Such a class should include: ash test, limit of starch in non-starchy drugs, limit of woody tissue in non-woody drugs, extraction constants, and clearer definitions.

The Medical Profession and the Pharmacopœia.—An editorial points out that: "A thoroughly up-to-date Pharmacopœia—one which will truly reflect the best medical practice of the present time—will contribute more to sane drug therapeutics than any other

one thing," and quotes Sollmann who suggests that: "If the Pharmacopœia is not and cannot be made practically important to physicians, then let us abandon it altogether."—*J. Am. M. Assoc.*, 1909, **53**, p. 1645.

Suggestions for the Pharmacopœia of the United States by Dr. Oliver T. Osborne, of Yale Medical School, have appeared in serial form, in recent numbers of the *Journal of the American Medical Association* (1910, **54**, pp. 50, 132, 208, 290, 376, 467). The author presents a number of really practical suggestions that are well worth careful consideration, but they are too numerous and too comprehensive to reproduce in abstract.

The National Formulary.—This book is also attracting considerable attention, and much valuable material is being presented in connection with the meetings of the local branches of the American Pharmaceutical Association. Among the more novel suggestions offered recently is one offered at the meeting of the Pittsburg Branch of the A. Ph. A. by Louis Emanuel, who proposes the introduction of a class of preparations designated "Vehiculæ" to be used as the name indicates, as vehicles for active medicaments.—*A. Ph. A. Bulletin*, 1910, February, p. 90.

The National Formulary Superfluous.—Donald McKesson is quoted as saying: "The N.F. as an official standard in prescribing the make-up of compounds hinders progress and improvement. It is only necessary that the ingredients be standard and the label correct and sufficiently descriptive. It is, of course, understood that some few of these compounds, by reason of popular and long usage, should be controlled and these might be properly introduced into the U.S.P.—*Drug Topics*, 1910, p. 19.

Digest of comments on the Pharmacopœia of the United States of America (eighth decennial revision) and the National Formulary (third edition) for the calendar year ending December 31, 1906, has just been published as *Hygienic Laboratory Bulletin* No. 58. The book comprises a total of 523 pages and includes a comprehensive review of the literature of 1906 relating to official articles. This bulletin is available to all who may be interested on application to the Surgeon-General of the Public Health and Marine-Hospital Service.

Reports of the Chemical Laboratory of the American Medical Association to January 1, 1909, and *Reports of the Council on Pharmacy and Chemistry* for 1905, 1906, 1907, and 1908 are two

small 8vo volumes of 84 and 207 pages respectively that contain much useful and interesting information relating to the composition of medicinal substances and the method of exploiting them. The information contained in these books should be of value to the pharmacist and the pharmaceutical chemist, and the two volumes might very properly find a place on the reference book-shelf of every pharmacy.

Among government publications that contain information of more than usual interest to the pharmacist are *Bulletin No. 61 of the Hygienic Laboratory* and *Bulletin No. 126 of the Bureau of Chemistry*. The former of these bulletins records quantitative pharmacological studies on the relative physiological activity of commercial solutions of epinephrine, by W. H. Schultz, and the latter (see *A. J. P.*, **81**, p. 420) contains a compilation of data on the "Harmful Effects of Acetanilid, Antipyrin, and Phenacetin," by L. F. Kebler, F. P. Morgan, and Philip Rupp. The latter bulletin has served to arouse renewed interest in the harmfulness of so-called "patent" medicines generally, and with other happenings of more recent date has served to call renewed attention to the responsibilities of the pharmacist in connection with the exploitation and sale of nostrums.

Up until quite recently it was generally supposed that retail druggists as a class recognized the mischief that could be and was being done by nostrums generally and that the continued sale of these articles in drug stores was at least largely due to the fact that patrons had become accustomed to purchase them, in connection with postage stamps and soda water, in the modern combination emporium known as a drug store. The development of a number of co-operative patent medicine manufacturing concerns has attracted the attention of medical men and the *Journal of the American Medical Association* has but recently (January 8 and 22, 1910) called attention to the methods of one of the larger of these concerns. The several editorials have attracted considerable attention, and in pharmaceutical circles have tended to show the existence of differences of opinion even among men of whom it might have been expected that they would be well informed in regard to the limitations of ready-to-take medicines.

That there are still many retail druggists in this country who are not willing to sacrifice honor for profit is evidenced by the open letter from Mr. Henry C. Blair, published in the *Pharmaceutical*

Era (February, 1910, p. 128) and by the reported action of the Philadelphia Association of Retail Druggists disavowing any interest, as an association, in the American Druggists' Syndicate.

British Pharmaceutical Codex.—This book, which has been out of print for some months since, is now in press and at a recent meeting of the Council of the Pharmaceutical Society it was announced that proof would soon be ready to submit to the Codex Revision Committee.

Pharmacopœia Suecica IX.—A review of the recent, ninth, edition of the Swedish Pharmacopœia calls attention to a number of more or less novel features. It appears that this Pharmacopœia has taken rather an advanced stand regarding active ingredients, and directs that for oil of anise or oil of fennel anethol be dispensed and that for oil of eucalyptus or oil of cajuput, eucalyptol be furnished.—*Apothek.-Ztg.*, Berl., 1910, **25**, p. 29.

New Hungarian Pharmacopœia.—A review of this, the third, edition of the Hungarian Pharmacopœia points out that the decree of the Minister of the Interior, bearing the imposing number 100,000, specifies that this book become the official authority on January 1, 1910. The book is printed in Magyar and in Latin, the two being bound together in a single volume. The work includes 526 official preparations and 106 reagents. The Latin nomenclature resembles that of the German and Austrian Pharmacopœias and the monographs generally suggest those included in the German Pharmacopœia. The decisions of the Brussels Convention have been closely adhered to and percolation has been generally adopted for preparing the tinctures of potent drugs. Specific gravity and extract content is specified for some tinctures and the alkaloid content is also specified in some instances. The list of appliances and utensils with which every pharmacy must be supplied includes: a distilling plant, a steam apparatus, a tablet machine, a sterilizer, and a compound microscope, magnifying at least 300 diameters.—*Chem. and Drug.*, Lond., 1910, **76**, p. 18.

New Italian Pharmacopœia.—The "Farmacopea Ufficiale del Regno d'Italia," III, is the first of the Continental pharmacopœias to be re-revised since the meeting of the International Conference in Brussels. It will perhaps be remembered that the second edition of the Italian Pharmacopœia was in press at the time and the Brussels Conference Protocol was therefore included as an appendix. In the present edition the several provisions of the protocol have been

quite fully embodied in the Pharmacopœia itself and each one of the included articles is specially designated (F. I.).

Centenary of the Journal de Pharmacie.—The centenary of the universally well known "Journal de Pharmacie et de Chimie, Paris," was recently celebrated by a dinner given at the Palais d'Orsay Hotel by Professor Jungfleish, president of the Editorial Committee of the journal, to his colleagues. The history of the journal was reviewed and its influence on the evolution of pharmacy in all portions of the world was commented on.—*Chem. and Drug.*, Lond., 1910, **76**, p. 37.

The Transactions of the Section on Pharmacology and Therapeutics of the American Medical Association, at the sixtieth annual session, held at Atlantic City, N. J., June 8 to 11, 1909, have just been published and constitute a large 8vo volume of 252 pages. Much of the material presented in this volume is of unusual interest to pharmacists, as it includes all of the papers and discussions on the Pharmacopœia that attracted such attention at the time. The book is printed by the American Medical Association Press, Chicago.

Serums and Vaccines.—A recent number of the *Journal of the American Medical Association* (Jan. 22, 1910) is devoted largely to a discussion of serums and vaccines, no less than eleven separate communications being included. For two of the preparations, vaccine virus and tetanus antitoxin, the plea is made that they should be included in the next edition of the U.S.P.

Serotherapy and the Pharmacopœia.—An editorial, commenting on the above series of papers on sera and allied products, calls attention to the great importance of these substances and the desirability of having a number of them recognized in the Pharmacopœia, with proper directions for their preservation and an enumeration of the precautions that are necessary to guarantee uniform efficiency.—*J. Am. M. Assoc.*, 1910, **54**, p. 295.

Vaccine Virus.—Dr. M. J. Rosenau believes that vaccine virus is deserving of official recognition because it is the oldest and best known specific preventive. It is a drug in the broadest sense of that term, and official recognition at this time would tend to establish for it an official and legal name and avoid future confusion with the bacterial vaccines and other so-called "vaccines" that are now being used in the prevention and cure of disease. Another advantage would be secured from the calling attention to the need for keeping this preparation in a uniformly cool place.—*Ibid.*, **54**, pp. 250–251.

Tetanus Antitoxin.—Dr. John F. Anderson describes the commercial preparations of tetanus antitoxin and calls attention to the variations in strength that were found before the general adoption of the American standard for determining the strength of this substance. He believes that this antitoxin is rightfully entitled to be included in future editions of the U.S.P.—*Ibid.*, **54**, pp. 253–254.

Physiological Testing of Ergot Preparations.—John C. Umney discusses the practicability of establishing a standard for preparations of ergot, and reports that three physiological experts gave widely varying opinions on a sample of fluidextract of ergot prepared from fine bold ergot by the B.P. method.—*Pharm. J.*, Lond., 1909, **73**, p. 794.

Physiological Standardization.—Alexander Goodall asserts that there is a growing recognition of the necessity for determining the activity and the probable strength of certain potent remedies whose active principles have hitherto successfully eluded the persevering researches of the chemist. Among the drugs that should be tested in this way he mentions squill, digitalis, strophanthus, cannabis indica, suprarenal substance, and ergot.—*Pharm. J.*, Lond., 1910, **74**, pp. 112–113.

Strophanthin.—Fleishmann and Wjasmenski (*Deut. med. Wchnschr.*, 1909, No. 21) report observations on 31 cases of intravenous injections of strophanthin gratus. While this method of administration is pointed out as being remarkably efficient, attention is also called to the fact that much care is necessary in the use of this remedy, as the therapeutic dose is dangerously near the toxic dose. The dose for an adult they give as 0.0005.—*Nouv. Remed.*, 1909, **26**, p. 517.

Digalen.—Worth Hale reports a comparative study of digalen and concludes that this article is not a uniformly stable preparation. Biologic tests also indicate that digalen is relatively much less potent than corresponding amounts of crystalline digitoxin but is of about the same activity as digitalein.—*J. Am. M. Assoc.*, **1910**, **54**, pp. 35–38.

Digipuratum.—The same investigator also reports a study of the comparative strength of digipuratum, said to be a purified extract of digitalis, and concludes that this preparation is of about the same activity as the strongest digitalis preparations on the market, but that it appears to offer no special advantages over standardized official preparations.—*Ibid.*, **54**, pp. 129–130.

Colocynth Constituents.—Power and Moore review the literature relating to the constituents of colocynth and report a comprehensive examination of Turkish colocynth. The seed represented 75.5 per cent. of the weight of the peeled fruit. They further demonstrate that the so-called colocynthin and colocynthitin, and perhaps other products heretofore obtained from colocynth and to which specific names have been attached, are indefinite mixtures, that the amount of glucosidic substance present in this drug is very small, and that the activity of colocynth is due to at least two principles, one of which is alkaloidal, although a very weak base, while the other is non-basic.—*Chem. and Drug.*, Lond., 1910, **76**, p. 150.

Refractive Indices of Essential Oils.—Ernest J. Parry, commenting on the refractive indices of essential oils, asserts that the refractometer is an absolutely necessary instrument in a laboratory where essential oils are examined, and points out that considerable information regarding the identity and composition of volatile oils can be obtained by the systematic examination of the several fractions obtained in the fractional distillation of an oil. He also enumerates the refractive indices of a number of essential oils, of the normal constituents, of adulterants, and of other liquids.—*Chem. and Drug.*, Lond., 1910, **76**, p. 178.

Cajuput Oil.—Baker and Smith report that a sample of oil of cajuput distilled from *Melaleuca uncinata* gave: specific gravity 0.9259, optical rotation $+7.2°$, refractive index 1.4788, saponification number 3.05, and solubility in 70 per cent. alcohol 1–15.—*Chem. and Drug.*, Lond., 1910, **76**, p. 151.

Medicinal Herbs.—To pharmacists and others who are interested in the cultivation and gathering of medicinal herbs, an illustrated article in the "Winter issue" of the *Chemist and Druggist* (Lond., 1910, **76**, pp. 179–182), describing the cultivation and the gathering of herbs in Kent, will prove to be more than usually interesting.

Veronal.—An abstract (from *Medical Press*) points out that an alarming number of deaths from the use of veronal, either by accident or intention, have been reported within the past few weeks, and the matter is pointed out as being well deserving of the serious attention of the government. In a recent veronal poisoning case at Cardiff the coroner expressed the opinion that there should be some legislation which, without interfering with the legitimate trade of the chemist, should form a protection for the public, so

that drugs like veronal could not be so easily obtained.—*Pharm. J.*, Lond., 1909, **83**, p. 690.

Adulterated Squill.—Karl Dieterich reports sorting over 20 kilos of squill and separating out upward of 1 kilo of fair-sized fragments of stone. This he thinks is too great a proportion to accept as being accidental.—*Pharm. Zentralh.*, 1909, **50**, pp. 971–972.

Echinacea.—A report of the Council on Pharmacy and Chemistry of the American Medical Association reviews the history and the uses of echinaceæ and points out that its use is characterized by an absolute lack of scientific scrutiny of the claims that have been made for it, and that until more reliable evidence is presented in its favor it is unworthy of consideration.—*J. Am. M. Assoc.*, 1909, **53**, p. 1836.

Sugar Production.—An abstract from the Board of Trade Journal gives the total sugar production of Europe during the season 1908–9 as being 6,487,000 metric tons as compared with 6,562,274 metric tons in 1907–8. The production of sugar in extra European countries is estimated at 7,765,500 metric tons, thus making a total sugar production for 1908–9 about 14,252,500 metric tons as compared with 13,911,655 metric tons in 1907–8.—*Pharm. J.*, Lond., 1909, **83**, p. 690.

Hydrogen Dioxide.—Endemann (*Annales de chimie analytique*) remarks that the acidity of this substance, when titrated with sodium hydrate, using phenolphthalein as an indicator, will vary with the age of the preparation. According to his observations the addition of sodium hydrate to an active solution of hydrogen dioxide tends to form NaOOH which does not give an alkaline reaction with the phenolphthalein. To obtain exact results he proposes adding an excess of alkali, heating to decompose the peroxide, and, after cooling, titrating back with solution of hydrochloric acid.—*J. de Pharm. d'Anvers.*, 1909, **65**, p. 863.

Gelatin, Sterilized Solutions of.—George P. Forrester points out that the possibility of gelatines harboring tetanus spores makes the preparation and use of solutions of gelatin a source of anxiety to the manufacturer and the physician. He outlines several methods for preparing solution of gelatin, including that of the Swiss Pharmacopœia, which provides for controlling the sterility of solutions of gelatin by injecting them into guinea-pigs and white mice.—*Pharm. J.*, Lond., 1909, **83**, p. 794.

Colors, Odors, and Flavors in Pharmacy.—These are discussed

by W. Gartside in a short paper in which he makes several practical suggestions. He concludes that for alkaline liquids carmine is a satisfactory red color, while for acids tincture of cudbear is to be preferred. For percolating cudbear he suggests the admixture of 50 per cent. of pine sawdust. For a brown color a solution of ordinary caramel is used, and for yellow he proposes a 4 per cent. tincture of saffron or a hydro-alcoholic solution of annatto. For blue a solution of indigo carmine is suggested, and for green a blending of the yellow with the blue. The suggestions for odors and flavors are also quite practical.—*Pharm. J.*, Lond., 1909, **83**, pp. 757–758.

Syrup of Wild Cherry.—Robert R. Hallaway reviews some of the recent literature relating to syrup of wild cherry, outlines a method for determining the hydrocyanic acid content of the bark and the resulting syrup, and concludes that not any of the recently described methods for making syrup of wild cherry extracts all of the available hydrocyanic acid.—*Ibid.*, **83**, p. 798.

Syrup of Wild Cherry.—J. C. Umney discusses the uses of syrup of wild cherry and points out that this preparation is largely employed as a vehicle for alkaloids such as heroin and codeine, and that these substances are naturally precipitated by the astringent syrup. He suggests that this difficulty might be overcome by a proper selection of the bark, and proposes that the Pharmacopœia include tannin limitation tests.—*Ibid.*, **83**, p. 800.

Opium Alkaloids in Preparations of Opium.—Van de Kreke and Swart report a comprehensive study to determine the degree of completeness with which morphine, narcotine and codeine are dissolved in making the several official galenical preparations. The opium used contained 14.7 per cent. of morphine, 3.83 per cent. of narcotine and 0.75 per cent. of codeine. Their results indicate that morphine readily goes into solution, either in an aqueous or an alcoholic menstruum, but that narcotine and codeine are but imperfectly dissolved by the former, while they are readily dissolved by an alcoholic menstruum.—*Pharm. Weekbl.*, 1909, pp. 1338–1342.

Ointments in Collapsible Tubes.—A rather ingenious contrivance for dispensing ointments in collapsible tubes is described and figured in a recent number of the *Pharmazeutische Zentralhalle* (1909, **50**, pp. 981–982). The essential feature of the scheme is to encase the ointment in impervious paper and to slide the ointment thus encased into the desired tube.

International Standards.—A. Schamelhout reports the Second International Congress for the Suppression of Fraud and comments at some length on the agreement reached in connection with the proposed international standards for drugs. Among these several standards are:

Aconite.—Dried aconite root should have a minimum of 0.5 per cent. of total alkaloids.

Aloes.—Good quality aloes should be at least 60 per cent. soluble in water and not yield more than 1.5 per cent. of ash.

Asafetida.—The portion of this drug insoluble in boiling alcohol, 90 per cent., should not exceed more than 50 per cent. of the total weight and the drug should not yield more than 20 per cent. of ash.

Balsam of tolu should not yield more than 1 per cent. of ash.

Benzoin.—Siam benzoin should not yield more than 2 per cent. of ash and not more than 10 per cent. of material insoluble in ether or alcohol.

Cantharides should not yield more than 9 per cent. of ash and should contain at least 0.5 per cent. of cantharidine.

Coca leaves should contain at least 0.5 per cent. of alkaloids.

Digitalis should be collected from wild growing plants.

Ergot should not yield more than 1.5 per cent. of ash and should contain at least 0.1 per cent. of alkaloids.

Adeps lanæ should not contain more than 0.2 per cent. of ash.

Codliver oil should have a specific gravity of from 0.920 to 0.930; iodine index, after four hours of contact, not below 140 and not above 170; and a saponification index of from 180 to 195.

Hydrastis should contain at least 2 per cent. of alkaloid.

Lycopodium should not yield more than 0.5 per cent. of ash.

Opium should contain at least 10 per cent. of morphine. When dried to a constant weight, at 60° C., should not lose more than 10 per cent. of weight. It should yield at least 45 per cent. of extract to water, equal to 38 per cent. of dry extract, and should yield not more than 6 per cent. of ash.

Rhatany should yield at least 12 per cent. of extract and yield not more than 5 per cent. of ash.

Scammony, Natural and Extracted.—Because of the difficulty presented by the selection of a satisfactory definition for scammony it was decided to postpone this for a future congress.—*Bull. Soc. Roy. de Pharm.*, Bruxelles, 1909, **53**, pp. 321–340.

BOOK REVIEWS.

FOOD INSPECTION AND ANALYSIS. For the use of Public Analysts, Health Officers, Sanitary Chemists, and Food Economists. By Albert E. Leach, S.B., Chief of the Denver Food and Drug Inspection Laboratory, Bureau of Chemistry, U. S. Department of Agriculture. Second edition, revised and enlarged. New York: John Wiley and Sons, 1909.

It is now five years since the first edition of this valuable work was published. During this time considerable progress has been made in food-control work, both in this country and Europe. The second edition reflects the progress that has been made, in that the changes and improvements have been incorporated in this volume. Of the chapters which have been revised, those treating of the following subjects may be mentioned: meats and meat extracts; flour (including methods for determining the grade and for the detection of bleaching); noodles and Italian pastes; paprika; prepared mustard; tea; coffee; cocoa products (including milk chocolate); ice cream; maple products; honey; oils (including the Polenske number and Bömers phytosterol-acetate test for vegetable oils); distilled liquors and preservatives (notably benzoic acid).

A valuable chapter on flavoring extracts has been introduced, including the examination of the lesser used extracts of almond, peppermint, wintergreen, rose, cassia, and cloves. A new chapter on the refractometer and its application in food analysis is also included. Much of the credit in bringing this new edition up to date is due to Dr. A. L. Winton, Chief of the U. S. Food and Drug Inspection Laboratory at Chicago.

The work comprises 21 chapters, including nearly 1000 pages, and an indication of its completeness may be had from an enumeration of the subjects treated: Food analysis and official control; the laboratory and its equipment; the functions, proximate components and nutritive value of foods; general analytical methods; the microscope in food analysis; the refractometer; milk and milk products; flesh foods; eggs; cereals and their products, legumes, vegetables and fruits; tea, coffee and cocoa; spices; edible oils and fats; sugar and saccharine products; alcoholic beverages; vinegar; artificial food colors; food preservatives; artificial sweeteners; flavoring extracts and their substitutes; and canned and bottled vegetables, relishes and fruit products. The work is illus-

trated with a number of drawings and about 40 plates of photomicrographs of pure and adulterated foods, and adulterants.

This book is indispensable to food and drug analysts, and besides the cause of pure foods will be materially assisted and advanced by its revision at this time. Analysts using this book are spared the trouble of looking up the literature except when some special question arises, and can devote most of their time to the analyses they have in hand. The preparation of the first edition no doubt contributed to the undermining of the health of the author, and while he has the satisfaction of having produced a work that is much appreciated, it will be some years before authors of such works are adequately rewarded.

TEXT-BOOK OF MEDICAL AND PHARMACEUTICAL CHEMISTRY. By Elias H. Bartley, Professor of Chemistry, Toxicology, and Pediatrics in Long Island College Hospital. Seventh revised edition, with ninety illustrations. Philadelphia: P. Blakiston's Son & Co., 1909. $3.00 net.

While the general character and form of Bartley's Chemistry is retained in the revised edition a number of changes have been made in the parts devoted to organic chemistry and physiological chemistry.

This is one of the best texts on medical and pharmaceutical chemistry published. The manner of presenting the subject is stimulating to the student, and the facts given are selected with a view of their practical application.

THE VEGETABLE PROTEINS. By Thomas B. Osborne, Ph.D., Research Chemist in the Connecticut Agricultural Experiment Station, New Haven, Connecticut. New York: Longmans, Green & Co., 1909.

This is one of the most commendable of the series of monographs on biochemistry being published by Longmans, Green & Co. Ten of these have already appeared, having been written by men who have gained an international reputation through their researches in their respective fields. The present monograph, dealing with vegetable proteins, is indeed welcome. Every student and reader on the subject of vegetable proteins has felt the need of the bringing together and correlating of the results of the various researches in a single volume.

In the present volume Dr. Osborne has devoted a limited space to a discussion of the general chemical and physical properties of the vegetable proteins. In eleven chapters covering about 100 pages, he gives a historical review of the proteins; the occurrence of proteins in the different parts of plants and their characteristics; the isolation and preparation of seed proteins; basic and acid properties of proteins; the solubility, precipitation, denaturing, physical constants, and products of hydrolysis of vegetable proteins; a classification of vegetable proteins; and some physiological relations of vegetable proteins to the animal organism, and the biological relations of seed proteins to one another. The book is enhanced by a very complete bibliography of over 600 references and has a good index.

THE EXTRA PHARMACOPŒIA OF MARTINDALE AND WESTCOTT. Revised by W. Harrison Martindale, Ph.D., F.C.S., and W. Wynn Westcott, M.B., Lond., D.P.H. Thirteenth edition. London: H. K. Lewis, 136 Gower Street, W. C., 1908.

This useful volume has undergone a thorough revision, many portions having been entirely rewritten. Among the new features may be mentioned: formalyzed gelatin as a substitute for collodions; glycetracta or glycerin extracts of drugs; the preparation of yellow mercuric oxide ointment; the organic (non-toxic) arsenic compounds; trypsin preparations, etc., etc. A number of new substances are considered. The recent literature has been carefully gone over and everything which is likely to prove of value to the pharmacist has been included.

E. MERCK'S ANNUAL REPORT, or Recent Advances in Pharmaceutical Chemistry and Therapeutics. 1908. Volume XXII. E. Merck, Chemical Works, Darmstadt, 1909.

This valuable annual report contains much information that is not to be found readily in any other publication. The first hundred pages are devoted to a consideration of organotherapy and organotherapeutic preparations. This presents an exceedingly interesting historical review of the subject, and also contains much of the newer matter relating to the organic preparations obtained from healthy animals. It is the most complete treatment of this subject that we have seen, giving the manner of preparation, physical and chemical properties, and the results of physiological and clinical tests of all

the substances that are used either on man or for experimental purposes.

Nearly 250 pages are taken up in a similar consideration of the results of scientific and clinical study of a large number of drugs and their preparations and of newer chemicals as well.

DIGEST OF COMMENTS ON THE PHARMACOPŒIA OF THE UNITED STATES OF AMERICA AND THE NATIONAL FORMULARY for the calendar year ending December 31, 1906. By Murray Galt Motter and Martin I. Wilbert. Washington: Government Printing Office, 1909.

This digest is issued as Bulletin No. 58 of the Hygienic Laboratory of the U. S. Public Health and Marine-Hospital Service, being published under the direction of the Surgeon-General with the approval of the Secretary of the Treasury. This bulletin embodies the second installment of the digest of comments on the U.S.P. VIII and the first digest of comments on the National Formulary (3d edition), this latter feature having been included at the request of the Council of the American Pharmaceutical Association.

The bulletin contains over 500 pages and includes about 5000 concise abstracts of the literature relating to the official articles published during 1906. The matter reviewed represents about 200 publications, including 18 foreign pharmacopœias. It is safe to say that nothing has ever been published which so completely covers the literature relating to the U.S.P. and N.F. for any one year. While the year 1906 will long be memorable in the minds of pharmacists and others by reason of the enactment of the National Food and Drugs Law, it also marked an era in pharmaceutical progress by virtue of the signing of the "Agreement between the United States and Other Powers respecting the Unification of the Pharmacopœial Formulas" by a diplomatic representative of the United States Government. It is, therefore, extremely fortunate that the complete literature for 1906 representing the views and practical results of the work of men engaged in or allied with pharmacy has been made available in the condensed form and admirable manner that it has in the Digest at hand. The abstracts are not only adequate but readable, suggestive, and indeed stimulating.

When the series of bulletins covering the literature up to the present year are all issued, they cannot fail to effect profoundly the practice of pharmacy. Investigations will be more fruitful; writers more careful; practices more modern; standards in the U.S.P. and

N.F. more exact, and drugs and their preparations more uniform and efficient.

Bulletin 58 is free to those interested in its contents, and may be had by application to the Surgeon-General of the Public Health and Marine-Hospital Service.

CORRESPONDENCE

UNITED STATES PHARMACOPŒIAL CONVENTION.

WASHINGTON, D. C., December 17, 1909.

TO THE ORGANIZATIONS AND INSTITUTIONS ENTITLED TO REPRESENTATION IN THE UNITED STATES PHARMACOPŒIAL CONVENTION, 1910:

For the first time in its history, the United States Pharmacopœial Convention will meet, on May 10, 1910, at Washington as a corporate body; it is therefore of the utmost importance that all the legal and constitutional requirements of the corporation be complied with. The response to the request for data, as to date of incorporation and period of continuous operation, has by no means been complete. Numerous requests have been received for credential blanks and forms for the notification of the appointment of delegates, and many of the notifications and credentials now in hand fail to meet the evident requirements of the Constitution and By-Laws of the Convention.

In order to secure uniformity as to these details and to provide that all the requirements of the Constitution be met, the Committee on Credentials and Arrangements has adopted the enclosed form, four copies of which will be sent to each organization or institution which, from information now at hand, is believed to be entitled to representation. These forms should be filled out carefully and completely, particularly with reference to the data as to date of incorporation and period of continuous operation; for it is highly desirable that these data of historical interest be a matter of record in the archives of the corporation, especially with reference to those organizations and institutions which, having been represented in the Convention of 1900, are, by special provision of the Constitution, entitled to representation in the Convention of 1910. One of these forms, after having been duly filled out, signed and sealed, should be sent to the Secretary of the Committee and another, like-

wise duly signed and sealed, should be given to *each* delegate, inasmuch as the By-Laws require that "*Every* delegate shall present his credentials to the Committee on Credentials and Arrangements." When the delegate registers at Washington on May 10, 1910, these latter forms will be exchanged for a registration and identification card. The blank, on the reverse side of the form, is left for notes by the Committee on Credentials and Arrangements or for a transfer of the credentials from the delegate to his alternate.

The Committee on Credentials and Arrangements is confident that, realizing the importance of these legal details of our corporate existence, even those organizations or institutions which may already have notified the Committee of the appointment of delegates, will be ready and willing to comply with this request and send to the Secretary of the Committee the new blanks completely filled out.

As in harmony with, and in further explanation of, Article I, Chapter VIII of the By-Laws, the Committee has decided that it cannot recognize the right of any one individual to represent more than one organization or institution.

Copies of the Constitution and By-Laws may be obtained on application to the Secretary of the Committee.

MURRAY GALT MOTTER, M.D.,
Secretary.

MINUTES, COMMITTEE ON CREDENTIALS AND ARRANGEMENTS, U.S.P.C.

PHILADELPHIA, PA.,
HOTEL BELLEVUE-STRATFORD,
27. XI. 09. 8.15 P.M.

1. The Committee on Credentials and Arrangements, of the United States Pharmacopœial Convention of 1910, was called to order by the Chairman, Dr. Oliver T. Osborne, of New Haven, Connecticut; there were present Messrs. Samuel L. Hilton of Washington, D. C., William L. Cliffe of Philadelphia, Pa., Dr. Horatio C. Wood, Jr., of Philadelphia, Pa., and Dr. J. H. Beal of Scio, Ohio; *ex officio* members: Dr. Henry M. Whelpley, Secretary, U.S.P.C. of St. Louis, Mo., and Dr. Murray Galt Motter, Assistant Secretary, U.S.P.C. of Washington, D. C.

2. On motion of H. M. Whelpley, seconded by J. H. Beal, Dr. Motter was made Secretary of the committee.

3. On motion, Messrs. Hilton and Motter were constituted a Sub-committee on Arrangements, with power.

4. On motion, the Chairman and Secretary were constituted a committee on the preparation of blank forms for the notification of the appointment of delegates, credentials, and identification cards; the suggestion that the form shown should contain an additional line in red ink giving further instructions being approved.

5. S. L. Hilton reported on the local arrangements already effected: hotel headquarters at the New Willard, with provision for general meeting room, committee rooms, lavatories, registration, hotel rates at eighteen different hotels, etc. On motion this report was approved.

6. The question of railroad rates and arrangements was left to the Sub-committee on Arrangements, with the suggestion that a conference be had with the proper officials of the Congress of American Physicians.

7. On the question of the interpretation of the Constitution and By-Laws, the committee holds that the terms of Sections 1 and 2 of Article II of the Constitution are quite explicit and clear in their definition of eligibility to membership in the Convention.

(a) The word "corporation" in Section 2, Article II, of the Constitution is interpreted to mean the Convention.

(b) The words "examined and acted upon as provided for by the By-Laws," mean certification to the Convention by the Committee on Credentials and Arrangements and the acceptance and approval of this committee's report by the Convention.

(c) The last sentence of Section 2, Article II, is held to be in no sense retroactive and to refer to the Convention of 1910 and Conventions thereafter.

(d) In order further to clarify the meaning of Article I, Chapter VIII of the By-Laws, particularly the last sentence, on motion of J. H. Beal, seconded by S. L. Hilton, the committee decided that it could not recognize the right of any one individual to represent more than one organization or institution.

8. On motion of S. L. Hilton, seconded by H. M. Whelpley, the list of organizations represented in the Convention of 1900, as printed in the U.S.P. VIII, is held to be authentic.

9. On motion of H. M. Whelpley the Secretary was requested to prepare the minutes of this meeting and a statement of such data as it might be advisable to publish which, after approval by the Chair-

man, are to be furnished to the medical and pharmaceutical press.

10. On motion of H. M. Whelpley, seconded by J. H. Beal, it was ordered that the list of delegates to be submitted to the Convention be published, in so far as it may then be completed, on April 1, 1910, with the explicit statement that such publication does not of necessity mean that such delegates will be received and seated by the Convention.

11. There being no further business, the Committee, on motion of S. L. Hilton, seconded by J. H. Beal, adjourned.

Attest: MURRAY GALT MOTTER,
Secretary.

AMENDMENTS TO THE CONSTITUTION.

WASHINGTON, D. C., Feb. 10, 1910.

TO THE MEDICAL AND PHARMACEUTICAL PRESS:

At a regular meeting of the Board of Trustees of the United States Pharmacopœial Convention held at Columbus, Ohio, January 28 and 29, 1910, it was resolved, five members of the Board of Trustees assenting thereto, to submit to the next meeting of the United States Pharmacopœial Convention (Incorporated) the following propositions to amend the Constitution of the Convention in the following particulars:

I. To amend Section 2, Article II, relating to membership, by inserting after the title "the Surgeon-General of the United States Marine-Hospital Service," the following: "the Secretary of Agriculture, the Secretary of Commerce and Labor, the Association of Official Agricultural Chemists, the Association of State and National Food and Dairy Department, the National Wholesale Druggists' Association, and the National Dental Association."

II. Also to amend said Section 2, Article II, by changing the words "three delegates" in line eleven (page seven of the reprint of the Constitution and By-Laws of 1909) to "one delegate"; the effect of this change being to reduce the representation of each organized body and department to one delegate each.

III. Also to amend Article IV, concerning "Committees and Trustees," by changing the title "Committee of Revision," to that of "General Committee of Revision" (Ibid., last line).

The Constitution does not require notice to be given of proposed changes in the By-Laws of the Convention, but to make

clear the purpose of the change proposed in the present title of the Committee of Revision it is hereby announced that the Board of Trustees will submit to the Convention propositions to amend the By-Laws as follows: to increase the number of members on the Committee of Revision, hereafter to be known as the "General Committee of Revision," from twenty-five to fifty, said General Committee of Revision to create from its own membership an Executive Committee of Revision of fifteen members, to have immediate charge of the work of revision, and also giving to said General Committee of Revision certain advisory and supervisory powers over the work of the Executive Committee of Revision.

MURRAY GALT MOTTER,
Secretary.

PHILADELPHIA COLLEGE OF PHARMACY.

SPECIAL LECTURES FOR 1909–1910.

THE TYPHOID ORGANISM AND ITS RELATION TO THE PUBLIC HEALTH.—Dr. A. C. Abbott, Director of the Laboratory of Hygiene, University of Pennsylvania, gave the fourth lecture of the course on Friday, November 19, at 3.30 P.M., his subject being "The Typhoid Organism and its Relation to the Public Health." The speaker was introduced by Mr. M. I. Wilbert, who remarked on the importance which is coming to be attached to the question of the economic value of health, and spoke of the fact that Dr. Abbott is a former student and follower of Dr. William H. Welch, one of the greatest minds devoted to medicine in the world.

Dr. Abbott's address furnished an excellent résumé of the subject.

He stated that typhoid fever should be of peculiar interest to Philadelphians for two reasons especially:

First, that it was in Philadelphia that a Philadelphia physician, Dr. Gerhard, demonstrated in 1836 that it was a distinct disease from typhus fever, with which it had heretofore been confused, and made it clear to the medical world that typhoid fever must be regarded as a pathological entity. This demonstration was made in the Philadelphia Hospital.

Second, that by the adoption of common-sense methods, thor-

oughly grounded in scientific investigation, it has been demonstrated in Philadelphia that typhoid fever may be practically eliminated as a serious disease of the people.

During the interval between these two discoveries practically all of our knowledge on this interesting subject has evolved, and it may be stated that the most important of our knowledge concerning prevention began with the discovery of the cause of the disease by Eberth in the year 1880. Following Eberth's discovery the great difficulty that was encountered was in the identification of the organisms that he claimed to be specifically answerable for typhoid fever, and this difficulty was not by any means lessened through the subsequent discovery of an organism in the intestinal canal that is in many particulars so like the typhoid germ as to make their separation more or less uncertain with the methods available at that time. This organism, the colon bacillus, has nothing to do, in so far as is known, with typhoid fever. It was pointed out that while these two organisms are not identical, yet botanically they have a close relation, and more recent studies have shown that there are thirty or forty organisms belonging to the typhoid-colon group which have been modified by their environment, as in the body of man, in culture media, and elsewhere. Dr. Abbott stated that no one, however skilled he may be, can identify the typhoid bacillus by means of the microscope alone, it being a simple rod-shaped organism like others of the group. The various attempts made with the object of devising methods for differentiating the *Bacillus typhosus* were described. Of these the agglutination test, which is based upon the condition that when an individual suffers from an infectious disease he becomes more or less immune to it, is the most reliable. Thus, if a beef-tea culture of typhoid bacilli, in which the organisms are in a motile condition, be added to the blood-serum of a person who has, or has had, typhoid fever, the organisms become immotile and massed together,—agglutinated,—while with a similar culture of the colon organism no such effect is produced. Dr. Abbott said that in the treatment of typhoid fever it is not possible to employ an antitoxic serum for the reason that the toxin is endotoxic, that is, closely bound up with the protoplasm of the cell (organism), and is only liberated when the latter is broken down, as in the digestion of the organisms by the leucocytes.

Then coming to the more practical side of the subject, Dr.

Abbott said that in order to ward off the disease it is necessary to have a knowledge of the manner of entrance and exit of the germs. He said that they are eliminated both in the fæces and urine, and that in many instances the urine of convalescents will show the presence of the bacilli, and that in a few well-authenticated cases the germs continued to be eliminated by the bowels throughout the remainder of the life of the individual, this period extending to forty years in one instance. The control of such cases offers considerable difficulty, but measures are being considered for looking after these so-called typhoid-carriers. It was stated that in order to contract typhoid fever the living germs must gain access to the alimentary canal, and in this connection it was pointed out that personal contact, such as handling a patient, may be sufficient to communicate the disease, and that the number of so-called personal-contact cases is larger than is usually suspected. As is well known contaminated drinking water and foods are also a source of the disease. Dr. Abbott said that when the outbreak of the disease is general, the water supply is usually the source of infection, and when it is restricted to certain areas or districts, as of a city, the milk supply may be suspected. Oysters were likewise mentioned as a source of the disease, and garden vegetables grown near cities on land fertilized with soil taken from the city were also considered to be a probable source of the disease. The house fly as one of the carriers of the disease received a share of attention. In all these instances infection is due to the direct or indirect transferral of the germs from human excreta, it being established that they are not propagated in the bodies of any of the lower animals mentioned. Thus, while the fly and the oyster may be carriers of the germs, they are not themselves the source of infection.

Dr. Abbott said that knowing the manner of elimination of the germs and the manner in which they are communicated, the methods of preventing infection readily suggest themselves. He said that those having the care of typhoid patients might look upon it as a safe rule that every time they place their hands upon the patient the hands became infected, and should be washed with soap and water. Another good rule is to cook all food, including milk, the statement being made that in many other countries milk is invariably cooked before being consumed. The necessity of thoroughly investigating the milk supply was emphasized, as milk is a good culture medium for the organism. Municipal cleanliness and a good water supply

were advocated as a matter of course. Still another method was suggested for combating the disease, namely, vaccination, and statistics were cited showing that where vaccination has been tried, as among the British soldiers in South Africa, Egypt, and India, the number of cases contracted was notably less, and that the mortality among the patients who were vaccinated was about half as great as among those not vaccinated.

Speaking of local conditions, Dr. Abbott said that before the filtration system was introduced for purifying the water supply of Philadelphia the annual number of cases of typhoid fever averaged about 6000, and in one year ran up to about 9000. With the introduction of filtration the number has been reduced about 80 per cent., the remaining 20 per cent. being due to infection from other sources, including the cases of summer vacationists who have contracted the disease elsewhere. During August, September, and October, about 50 per cent. of our cases are traced to outside sources of infection.

With regard to the determination of the presence of typhoid organisms in water supplies, Dr. Abbott stated that the time required for the disease to manifest itself after infection is about three weeks, and that as the germ does not live long in water it is usually not present when examinations are made, and that it is much better to judge of the situation by a direct examination of the surroundings. He said with reference to the inferential test that when the colon organism is found in water the presence of the typhoid organism is indicated, that too much reliance could not be placed upon it, as the colon organism is found in the intestinal tract of all domestic animals, and as these do not suffer from typhoid fever the colon organism is likely to be found in places where the typhoid germs are not present, and that the fact of the presence of the colon organism must be considered along with other available data. F. Y.

THE MANUFACTURE AND TESTING OF MEDICINAL PLASTERS was the subject of an illustrated address given on Friday, December 10, at 3.30 P.M., by F. B. Kilmer, chemist for Messrs. Johnson & Johnson, of New Brunswick, N. J., one part of which appears in this issue (p. 112) and the remainder of which will be published in a later number of this JOURNAL. The speaker was introduced by Mr. Warren H. Poley, a member of the Lecture Committee, who recounted some of his earlier experiences in the handling and spread-

ing of plasters. At the close of the lecture Prof. Joseph P. Remington thanked Mr. Kilmer on behalf of the College and the classes, stating that he had always found him willing to give information on any subject with which he was familiar. Among the visitors in attendance were Dr. John F. Hancock, of Baltimore, and Mr. Otto Raubenheimer, of Brooklyn. F. Y.

TRYPANOSOMES AND TRYPANOSOMIASES (the Sleeping Disease and its Causes).—The foregoing was the subject of the sixth lecture, which was delivered on Friday, December 17, by Dr. Leonard G. Rowntree, instructor in pharmacology and experimental therapeutics at Johns Hopkins University. The lecturer was introduced by George M. Beringer, who said that the committee had chosen rather a wide range of subjects for this series of lectures, believing that the pharmacist should know something more than pertains directly to his calling.

Dr. Rowntree stated that in both Germany and England commissions had been appointed to consider the problems involved in the cure and control of the diseases due to trypanosomes, while in this country the subject has been taken up by the universities. The trypanosomes are microscopic parasites belonging to that branch of the animal kingdom known as Protozoa, and the diseases set up by the pathogenic forms of this group are known as trypanosomiases. A number of species of this protozoon has been described, the organisms varying from 24 to 75 microns in length. They are characterized by the presence of a nucleus, a centrosome, chromatic granules, and a flagellum. They are very active, having several movements, and reproduce by division, starting at the centrosome. They derive their nutrition by osmosis, and multiply very rapidly, an infected animal showing the presence of millions of the organisms in a few hours, as in the case of the rat. In 1841 the first trypanosome was described, and in 1901 Dutton found a patient in Gambia whose blood showed the presence of a trypanosome, which was later proven by Castellani, Bruce, Nabarro, and Low to be the cause of the sleeping sickness. Dr. Rowntree described some six diseases which affect the lower animals due to different species of trypanosomes: (1) one, *Tryp. Lewisi,* affecting rats in all countries, including America; (2) a disease in Africa, *nagana,* in the communication of which the tsetse-fly plays a part and which affects cattle, horses, and dogs, but not man, and is supposed to have come originally from wild animals as alligators and rhinoceri; (3) a disease in India,

known as *surra,* affecting horses and camels, the latter being more resistant to the disease and carrying it over from one season to another; (4) a disease affecting horses in South America due to an organism communicated by flies and supposed to have been brought originally from an island at the mouth of the Amazon, a large rodent or rat probably having been the original host; (5) another disease, *Dourine,* affecting horses in Africa and first found in Europe along the Mediterranean coast, and which at one time reached this country, it being found among the horses in Wyoming and one of the Dakotas; (6) still another disease affecting cattle in South Africa, one peculiarity of which is that the native-born cattle are immune to a certain extent.

Then, referring more especially to sleeping sickness, Dr. Rowntree stated that in 1803, just 100 years before the finding of the organism causing the disease, Winterbottom described it as it occurs among the colored people in Africa. He said that the centre of infection extends from Lake Nyanza up to the Nile and over to the Congo, where 73 per cent. of the population has been wiped out. In Uganda some 500,000 of the inhabitants died from the disease in the past five or six years. In describing the course of the disease, Dr. Rowntree stated that it is at first exceedingly insidious, and that one fly (*Glossina palpalis*) constitutes the intermediate host. The disease seems to have a predilection for the nervous and lymphatic systems, and the organisms have been found in the fluid of the lymph-glands and in the cerebrospinal fluid.

Up to the present time arsenic has played the most important part in the treatment of all of these diseases. Both its inorganic compounds and organic derivatives are used, as arsenic trioxide, arsenites, Donovan's solution, atoxyl (sodium p-aminophenyl arsonate). The idea in the treatment of trypanosomiasis is to administer a remedy which is taken up more readily by the parasite than by the host, as suggested by Thomas, and Ehrlich has found that arsacetin (an acetyl derivative of atoxyl) is 1500 times less toxic to the affected organism than arsenic itself. Another compound recently tried by Ehrlich which promises well is phenyl-arseneglycine, though, as stated by Dr. Rowntree, it is yet far from ideal. Among the other remedies which have been tried are trypan red and other dyes, such as malachite green, and preparations of mercury and antimony. To Koch also belongs much credit for the

knowledge gained in the treatment of this disease, he having gone to Africa to study it at first hand.

The European has been found to be susceptible to the disease as well as the negro, and along the shores of Lake Victoria-Nyanza the governments are co-operating with a view of stamping it out, having already adopted certain restrictive or quarantine-like measures. The disease furnishes three points of attack, namely, the patient, the fly and the organism (trypanosome). F. Y.

PLANTS INJURIOUS TO ANIMALS formed the title of the seventh lecture of the series, which was delivered on Friday, January 7, at 3.30 P.M., by Dr. C. Dwight Marsh, of the Bureau of Plant Industry, U. S. Department of Agriculture, Washington, D. C., who spoke in place of Dr. Rodney H. True, who was prevented from being present. Dr. C. A. Weidemann presided, and at the close of the address, said, after thanking Dr. Marsh for the information given, that he had gotten a broader view of what the government is doing for the people of this country.

Dr. Marsh said that the government had been engaged in an investigation of the loco-disease, which causes such heavy losses to stockmen on the grazing lands of the Great Plains east of the Rocky Mountains, for some years past. Of the plants causing the disease he mentioned the following: *Zygadenus elegans,* injurious to sheep; the larkspurs or Delphiniums causing losses among cattle; and lupines causing losses among sheep and also horses. The attention of the government workers was, however, confined mostly to the two plants, *Aragallus lamberti* and *Astragalus mollissimus,* these causing greater loss than all other poisonous plants combined, and having come to be regarded as the loco-plants par excellence. Both plants belong to the *Leguminosæ. Aragallus lamberti,* also commonly known as "rattleweed" or "white loco," has a wide range, extending from Alaska on the north down through the whole grazing region of the Great Plains where it is very abundant. *Astragalus mollissimus* ("purple loco," "woolly loco," or "Texas loco") is more limited in its range.

The word "loco," meaning crazy, is of Spanish origin, and is applied in reference to the peculiar nervous symptoms manifested by the affected animals. Dr. Marsh stated that at the time the government experiments were begun, it had not been definitely determined that the loco-disease was due to the loco-plants, a number

of theories having been advanced as to the cause of the disease, although the evidence, including the results of pharmacological experiments by Dr. Mary G. Day, pointed strongly in this direction. The feeding experiments carried on by the government both under corral conditions and in the open, in which the loco-weeds constituted a part of the food on the one hand and were rigidly excluded on the other, have proved conclusively that the disease is due to loco-plants. The course of the disease, which is characterized by marked nervous symptoms, anæmia, and general debility, was described, as were also experiments in the treatment of the disease. As a result of these experiments it was found that Fowler's solution in daily doses of 15 c.c. continued for about one month is the best remedy for locoed horses, and that for cattle daily doses of 0.009 to 0.012 Gm. of strychnine, or daily doses of 0.4 Gm. of sodium cacodylate, given hypodermically, and continued for a period of one or two months constitute the most reliable remedy. It was noted that the locoed animals are especially susceptible to the usual veterinary doses of the medicines named, and hence it was found necessary to administer them in the small doses given. Laxative agents were also found to be an essential feature of the treatment, laxative foods and magnesium sulphate being recommended in this connection.

Dr. Marsh stated that the loco-plants can be destroyed by digging them up, and that this is a feasible practice in some localities.

F. Y.

PHYSIOLOGICAL ASSAY: ITS VALUE AND LIMITATIONS.—This was the subject of the eighth lecture, which was delivered on Friday afternoon, January 21, by Dr. Horatio C. Wood, Jr., associate professor of pharmacology, University of Pennsylvania. The speaker was introduced by Prof. Henry Kraemer who said that there is no subject which should be of more concern to the pharmacist than the efficiency of the preparations which he dispenses, and that therefore every method which promises to be of value, either in the testing of medicines or which will aid in establishing their value, must necessarily be of special interest to him. (See page 101.)

F. Y.

AMERICAN PHARMACEUTICAL ASSOCIATION.

The officers of the Section on Scientific Papers would again remind you that the annual meeting of the American Pharmaceutical Association to be held in Richmond, Va., the week following May 2, 1910, offers the last and in many respects the most favorable opportunity to discuss matters of scientific interest in connection with the Pharmacopœia of the United States previous to the meeting of the Pharmacopœial Convention to be held in Washington, May 10, 1910.

To insure profitable and comprehensive discussions, it will be necessary to limit the number of communications presented at each session, and, as the sessions themselves are in turn limited, the committee would request that all members of the association who are interested in the work of the Section on Scientific Papers will promptly announce their willingness to contribute to the programme and indicate, approximately, the time that they will require to present their communications.

Communications to be printed in advance of the meeting should be in the hands of the printer at least six weeks in advance of the date of the annual meeting, and titles with the accompanying abstracts to be included on the programme should be in the hands of the Chairman of the Section at least one month in advance of the meeting.

M. I. WILBERT,
Chairman.

The meeting of the City of Washington Branch of the American Pharmaceutical Association, February 2, 1910, was devoted to a discussion of the report of a special Committee on National Formulary. On motion, the following principles were endorsed:

Object.—The National Formulary should be a book of remedies which not only conserve and protect the welfare of the people, but also represent the best that the American Pharmaceutical Association stands for.

Nomenclature.—No name should be used which misleads in any particular.

Standards.—It is believed that it would be preferable to have a definite standard prescribed, when practicable, for each product recognized.

Division of Book.—It is unwise to divide the book into two parts.

Introductory Notes.—The National Formulary should include useful introductory notes, comments, etc.

Metric System.—The metric system alone should be employed in giving the quantity or proportion to be used in preparing the various products.

Medicinal Tipples.—All products which bear any form of stigma characterizing tipples should be eliminated.

Saccharin.—The use of saccharin as a sweetening agent for National Formulary products should be discouraged.

Pills.—The general direction for making and coating pills should be continued if it is found practicable to present the matter in an intelligible form.

Artificial Coloring.—The artificial coloring of official preparations should be discouraged; it is desirable, however, to introduce one or more formulas for preparing coloring solutions to be used when called for by prescriptions.

Preservatives.—Preservatives, other than such articles as alcohol and glycerin, should not be used in pharmaceutical preparations.

Basic Elixirs.—The introduction of several select basic elixirs is recommended.

Proprietary Medicines.—Formulas intended to produce an imitation of some proprietary product should not be included in the National Formulary.

Supplements.—Supplements, corrections, and additions should be issued as the progress of pharmacy and medicine may demand.

On motion, it was agreed that the paragraphs endorsed by the members present be submitted to the Committee on National Formulary.

Saccharin.—Saccharin was discussed at some length, and it was suggested that because of the wide-spread use of this article and the apparent difference of opinion regarding the possibility of harm resulting from its use, additional information be sought regarding it, and on motion of Mr. Flemer, seconded by Mr. Hynson, the following resolution was adopted.

Resolved, by the City of Washington Branch of the American Pharmaceutical Association, that, in view of the extensive use of saccharin and the possibility of harm arising from such use, the matter is referred to the Surgeon-General of the Public Health and Marine-Hospital Service with the request that it be made the subject of pharmacologic investigation.

M. I. WILBERT,
Secretary.